NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Betrixaban for preventing venous thromboembolism in people hospitalised for acute medical conditions

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of betrixaban within its marketing authorisation for preventing venous thromboembolism in people hospitalised for acute medical conditions.

Background

Venous thromboembolism is a term used to describe deep vein thrombosis and pulmonary embolism. Deep vein thrombosis is the formation of a thrombus (blood clot) in a deep vein, usually of the lower limbs. When deep vein thrombosis occurs, dislodged thrombi may travel to the lungs and this is called pulmonary embolism. Pulmonary embolism can cause sudden death, and those who survive a pulmonary embolism occasionally require intensive care and recovery can take several weeks or months. Other complications of deep vein thrombosis include post-thrombotic syndrome, a chronic disorder that may include symptoms such as pain, heaviness, swelling, cramps, itching or tingling, increased skin pigmentation and ulceration in the affected limb. In addition, chronic thromboembolic pulmonary hypertension is a rare but potentially treatable consequence of pulmonary embolism.

Venous thromboembolism has an annual incidence of approximately 1 in 1000 of the general population in England[1], This rate varies substantially with age[2]. Approximately half of all cases are associated with hospitalisation, with many events occurring up to 90 days after admission[3]. Key risk factors for patients admitted to hospital include age over 60, recent immobility due to illness, prior venous thromboembolism, active cancer, obesity, sepsis and exacerbation of inflammatory illness, chest disease and heart failure.

Prevention of venous thromboembolism in patients admitted to hospital for medical care involves assessing the patient's risk of developing the condition and applying appropriate prophylactic interventions. For people considered at high risk of developing venous thromboembolism and low risk of bleeding, NICE clinical guideline 92 recommends fondaparinux sodium, low molecular weight heparin or unfractionated heparin (for patients with severe renal impairment or established renal failure). Where the risk of bleeding is higher than the risk of venous thromboembolism, the guideline recommends mechanical prophylaxis such as anti-embolism stockings, foot impulse devices, and intermittent pneumatic compression devices. NICE medical technology guidance 19 states that the geko device (a neuromuscular electrostimulation device) can be used to reduce the risk of venous

thromboembolism for people in whom it is not possible to use other methods of preventing blood clots.

The technology

Betrixaban (brand name unknown, Portola) is an anticoagulant that acts by direct inhibition of activated factor X (factor Xa). Factor Xa is a key component in the formation of blood clots. Betrixaban is administered orally.

Betrixaban does not currently have a marketing authorisation in the UK for preventing venous thromboembolism. It has been studied in a clinical trial in the hospital and post-discharge period, compared with enoxaparin, for preventing venous thromboembolism in people aged 40 years and over. Patients in the trial were hospitalised for an acute medical condition including congestive heart failure, acute respiratory failure, acute infection without septic shock, acute rheumatic disorders, and acute ischaemic stroke with lower extremity hemiparesis or hemi paralysis.

Intervention(s)	Betrixaban
Population(s)	Adults who are hospitalised for an acute medical condition and are at risk of venous thromboembolism
Comparators	• fondaparinux sodium • low molecular weight heparin • unfractionated heparin (for patients with severe renal impairment or established renal failure)
Outcomes	The outcome measures to be considered include: • mortality • incidence of deep vein thrombosis • incidence of pulmonary embolism • adverse effects of treatment including bleeding events • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals 'Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism' (2012). NICE Technology Appraisal 261. Guidance on static list. 'Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism' (2013). NICE Technology Appraisal 287. Guidance on static list. 'Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism' (2014). NICE Technology Appraisal 327. Review date December 2017. 'Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism' (2015). NICE Technology Appraisal 341. Review date June 2018. 'Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism' (2015). NICE Technology Appraisal 354. Review date August 2018. Related Medical Technology Guidance 'The geko device for reducing the risk of venous thromboembolism' (2014). NICE Medical Technology Guidance 19. Related Guidelines: 'Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients

	admitted to hospital' (2010). NICE guideline 92. Update in progress, publication expected Feb 2018. 'Venous thromboembolic diseases: the management of venous thromboembolic diseases and the role of thrombophilia testing' (2012). NICE guideline 144. Updated Nov 2015. Related Quality Standards: 'VTE prevention' (2010). NICE Quality Standard 3. 'Diagnosis and management of venous thromboembolic diseases' (2013). NICE Quality Standard 29. Related NICE Pathway: 'Venous thromboembolism'. NICE Pathway.
Related National Policy	NHS Commissioning Board (2013) 'Commissioning for quality and innovation (CQUIN): 2013/14 guidance'. Section 8. NHS England (2013) 'NHS England Guidance for Commissioners: Commissioning Services that deliver high quality VTE prevention'. Department of Health (2014) 'NHS Outcomes Framework 2015-2016'. Domains 1, 2, 3, 4 and 5. NHS England (2015) 'NHS England National VTE Prevention Programme'.

Questions for consultation

Have all relevant comparators for betrixaban been included in the scope? Which treatments are considered to be established clinical practice in the NHS for preventing venous thromboembolism in people who are hospitalised for an acute medical condition? Are warfarin and the newer oral anticoagulants such as rivaroxaban, dabigatran etexilate, apixaban and edoxaban used in clinical practice for this indication?

Are there any subgroups of people in whom betrixaban is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider betrixaban will fit into the existing NICE pathway, venous thromboembolism?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the

proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which betrixaban will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider betrixaban to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of betrixaban can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

1. House of Commons Health Committee (2005) 'The prevention of venous thromboembolism in hospitalised patients'. Accessed April 2016

2, Scottish Intercollegiate Guidelines Network (2010) 'Prevention and management of venous thromboembolism (quick reference guide SIGN 122)'. Accessed April 2016.

3. Venous thromboembolism. NHS Choices. Accessed April 2016